Remarks

Claims 1-21, 24-26 and 28 were pending in the subject application. By this Amendment, claim 25 has been amended, claims 1-21, 24, 26 and 28 have been cancelled and new claims 29 and 30 have been added. No new matter has been added by these amendments. Accordingly, claims 25, 29 and 30 are before the Examiner for consideration.

The amendments to the claims have been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. These amendments should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claims 2 and 26 have been objected to due to a typographical error. By this Amendment, the applicants have cancelled claims 2 and 26 thereby rendering moot this objection.

Claims 25 and 26 have been rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. The applicants respectfully traverse this ground for rejection because the applicants' disclosure provides clear evidence that the applicants were in possession of the subject invention at the time of filing their application.

Please note that claim 26 has been cancelled herein and 25 has been amended to lend greater clarity to the claimed subject matter. Specifically, claim 25 now recites that the additional component of the combination therapeutic is peripheral tryptophan hydroxylase.

The Office Action distinguishes the applicants' claimed second protein from the recitation of an acceptable carrier or excipient by saying that the applicants' second protein is "important." The applicants agree that the second constituent of the combination therapeutic is important. However, the applicants do not agree that this necessitates providing a specific structure in order to satisfy the written description requirement.

First, the applicants are not sure that they agree with the implication that a carrier or excipient is not important. Furthermore, it is unclear how the "importance" of a component affects whether the inventors had possession of that embodiment as claimed.

The Office Action goes on to suggest that the "genus" of tryptophan hydroxylases is "broad" and "structurally diverse." No support is given for these statements other than reference to possible "mutants" and "variants." If one were to accept this line of reasoning, then nothing could ever be claimed based on its function because everything can potentially be modified and the modified thing may or may not retain the activity of the original thing.

Recent court decisions have made it clear that compliance with the written description requirement does not require the type of disclosure that has been set forth as necessary in the outstanding Office Action. See, for example, Capon v. Eshhar, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005).

The combination therapeutic as now claimed is based on the identification of a new use for the SEQ ID NO:2 protein. Having knowledge of this new use, the inventors also envisioned the use of this protein with other proteins for regulating serotonin metabolism, including peripheral tryptophan hydroxylases. These other proteins are not being claimed; rather it is merely their use in combination with the protein of the subject invention that is being claimed. Tryptophan hydroxylases would be known to, and readily envisioned by, those skilled in the art having the benefit of the current disclosure.

In the current case the applicants have merely referred to well-known proteins that would be readily recognized by those skilled in the art — including the inventors. Nothing more is necessary to establish that the inventors had "possession" of this embodiment as required by 35 U.S.C. §112.

Because the applicants were in full possession of the claimed invention at the time of filing, the applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §112, first paragraph.

Claims 2, 25 and 26 have been rejected under 35 U.S.C. §112, first paragraph, under the enablement requirement. The applicants respectfully traverse this ground for rejection to the extent that it might be applied to the claims now presented for examination.

Please note that the applicants have amended claim 25 herein to recite 95% homology to the exemplified sequence. Support for this amendment can be found at, for example, page 7, first full paragraph of the specification as filed. Given the high level of skill in this art, as well as the

guidance provided in the applicants' specification, a person skilled in the art could readily practice the subject invention with closely-related sequences as now claimed.

Accordingly, the applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. §112, first paragraph.

Claims 2 and 3 have been rejected under 35 U.S.C. §102(b) as being anticipated by Yu *et al.* (WO/2002/97039). The applicants have cancelled claims 2 and 3 thereby rendering moot this ground for rejection.

Claims 25 and 26 have been rejected under 35 U.S.C. §103(a) as being obvious over Yu *et al.* (WO 2002/97039) as applied to claims 2-3 above and in view of Wang *et al.* (J. Neurochem. 1998) and Veenestra-VanderWeele *et al.* (Mol. Interv. 2003, 72-5, 50 Review). The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not disclose or suggest the applicants' invention as claimed.

WO 2002/97039 merely discloses proteins that "share structural similarity with animal hydroxylases, and particularly tryptophan hydroxylases, which are involved in a rate-limiting step in the biosynthesis of a number of neurologically active compounds, including, but not limited to, DOPA, serotonin and melatonin" (page 2, lines 1 – 5).

WO 2002/97039 does not disclose any biological data verifying the function of the proteins. More importantly, in addition, it is nowhere stated that the polypeptide depicted in SEQ ID No. 2 functions as a neuronal tryptophan hydroxylase (snTPH).

The present application teaches that serotonin is independently synthesised by two different tryptophan hydroxylase isoenzymes in the peripheral tissues and in the neurones. The inventors of the present invention have succeeded in providing nucleic acid molecules encoding a protein with the enzymatic activity of a neuronal tryptophan hydroxylase (snTPH).

In contrast, the protein of WO 2002/97039 is only *assumed* to have a general tryptophan hydroxylase activity, wherein there is no distinction between peripheral and neuronal tryptophan hydroxylase activity. Thus, WO 2002/97039 fails to disclose or even suggest that SEQ ID No.2 is a specifically neuronal isoform of tryptophan hydroxylase. Without this knowledge there would be no reason to propose the combination therapeutic composition as set forth in claim 25.

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.*

The secondary references cited in support of this obviousness rejection do not cure or even address the aforementioned deficiencies of the primary reference. Specifically these references do not disclose or suggest that SEQ ID NO:2 is a neuronal tryptophan hydroxylase. Without this knowledge there would be no reason to produce the combination therapeutic now claimed.

An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using the applicant's disclosure to reconstruct the prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Sponnoble*, 56 CCPA 823, 160 USPQ 237,243 (1969). The cited references, either alone or in combination, do not provide a suggestion of the claimed invention and, certainly, no expectation of success. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) based on Yu *et al.* in view of Wong *et al.* and Veenestra-VanderWeele *et al.*

In view of the foregoing remarks and the amendment above, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

David Saliwanchik

David R. Saliwanchik
Patent Attorney
Registration No. 31,794
Phone: 352-375-8100
Fax No.: 352-372-5800
Address: P.O. Box 142950
Gainesville, FL 32614-2950

DRS/la